REMARKS

This amendment is submitted in an earnest effort to bring this case to issue without delay.

Applicants wish to reiterate their claim to the benefit of their Hungarian priority date of 20 September 2002 pursuant to the International Convention. A certified copy of Hungarian Patent Application P0203114 filed 20 September 2002 has been made of record as part of Applicants' PCT/HU2003/000072 filed 18 September 2003 of which the instant application is the US National Phase. The Examiner has already acknowledged Applicants' perfected right of priority.

Applicants are submitting a substitute specification in which the structural formulae, provided as a chart at the end of the application as filed, have now been integrated into the application. Furthermore the substitute specification contains the headings normally required under US Patent Practice. Applicants have inserted no prohibited nee matter into the substitute specification.

Applicants note that the original claims filed in this application are claims 1 through 8. Applicants have canceled those claims and are submitting new claims 9 through 18. Antecedent basis for all of the new claims may be found in the specification on page 2, line 25 through page 4, line 15, and in the specific examples. Thus claims 9 through 18 are now in the application and are presented for examination.

All claims now presented include the respective structural formulae (I) through (IV) and thus are believed to be in full compliance with the requirements of 35 USC 112, second paragraph.

Applicants appreciate the Examiner's indication that claims 1 through 7 originally presented contain allowable subject matter. Applicants have canceled claims 1 through 7 and replaced those claims with new claims 9 through 16. New claims 9 through 16 cover the same subject matter originally covered by claims 1 through 7. However, new claims 9 through 16 contain the structural formula of the compounds integrated into the body of the claims. There is no disclosure or suggestion in the prior art of the one-pot process according to the present claims to obtain lamotrigine.

The Examiner has rejected claim 8 last presented as obvious under 35 USC 103 citing GUNTOORI et al US Patent 6,586,593. The Examiner points to Procedure I and Procedure III in cols. 5 and 6 of the reference and contends that the presently claimed intermediate of the Formula (III) is made according to these processes. There is no isolation of the aminoguanidine dimesylate of the present Formula (III) according to GUNTOORI et al. However, the Examiner contends that one "skilled in the art" would be motivated to use the isolated aminoguanidine dimesylate in the same way that the unisolated, formed in situ version of the salt is used in Procedures I and III of the reference. Thus the Examiner considers that the intermediate of the Formula (III) is obvious and unpatentable.

Applicants strongly believe that no refusal of claims 17 and 18 should be maintained as obvious under 35 USC 103 in view of the cited reference. Applicants find nothing in the GUNTOORI et al reference that would motivate one "skilled in the art" to replace Procedure I or Procedure III of GUNTOORI et al with the present process where aminoguanidine dimesylate is formed and isolated before reacting with 2,3-dichlorobenzoyl cyanide to form the Formula (IV) adduct. The aminoguanidine dimesylate is only an intermediate and there would be no reason to believe that isolation of the aminoguanidine dimesylate in advance of the reaction with 2,3-dichlorobenzoyl cyanide would improve the yield or purity of the lamotrigine final product if the aminoguanidine dimesylate is first isolated according to the present invention before the reaction with 2,3-dichlorobenzoyl cyanide to form the adduct of the Formula (IV).

The Examiner seems to indicate his belief that one "skilled in the art" would expect no difference in the yield or the purity of the lamotrigine final product or any other benefit whether the aminoguanidine dimesylate is first isolated according to the present invention before the reaction to form the compound of the Formula (IV) and eventually the compound of the Formula (I). Applicants point out, however, that the invention is not just the advance preparation and isolation of the aminoguanidine dimesylate, but also includes the formation of a suspension of the aminoguanidine dimesylate in methanesulfonic acid and adding 2,3-dichlorobenzoyl cyanide to this system to form the adduct of the

Formula (IV). Applicants find no suggestion of same in GUNTOORI et al and nothing disclosed therein to motivate one "skilled in the art" to form the aminoguanidine dimesylate in advance of the reaction with 2,3-dichlorobenzoyl cyanide, to isolate the aminoguanidine dimesylate, or to form a suspension of the isolated aminoguanidine dimesylate in methanesulfonic acid and then adding thereto 2,3-dichlorobenzoyl cyanide to form the Formula (IV) adduct.

Furthermore the product of Procedure I and Procedure III in GUNTOORI et al is not lamotrigine, but is lamotrigine monohydrate. A subsequent drying step is needed according to Procedure IV of the reference to remove the water of hydration from the lamotrigine monohydrate to obtain lamotrigine. No such drying step is required in Applicants' presently claimed process proceeding through Applicants' novel intermediate salt of the Formula (III). There is no suggestion in GUNTOORI et al or in any other prior art reference that one can dispense with the subsequent drying step to convert the lamotrigine monohydrate to obtain lamotrigine by proceeding through the use of the isolated intermediate of the Formula (III) of new claim 17, preferably in the form of the suspension that is the subject of new claims 18. Accordingly no claim now presented should be rejected as obvious under 35 USC 103 in view of the reference.

Applicants now have the following direct comments regarding the patentability of new claims 17 and 18 directed to the

new intermediate salts of the Formula (III) isolated or in the form of a suspension in methanesulfonic acid:

Applicants' formation of a suspension of the aminoguanidine dimesylate in methanesulfonic acid to then form the adduct of the Formula (IV) by reacting the suspension with 2,3-dichlorobenzoyl cyanide results in obtaining the lamotrigine in high yield and purity by transforming the Formula (IV) adduct with magnesium oxide without the need for a drying step. The formation of the Formula (IV) adduct is surprisingly fast and is surprisingly almost quantitative (see page 2, last paragraph of the original specification). From the lamotrigine one can easily obtain the Formula (IV) adduct, and the final product is substantially free of by-products. There is no suggestion in GUNTOORI et al to either form or use aminoguanidine dimesylate in such a way.

From reading GUNTOORI et al, there is no evidence that GUNTOORI et al recognized the importance of isolating aminoguanidine dimesylate, and using the isolated salt to help obtain the final product in high yield and purity, instead they only described aminoguanidine salts in general terms. One "skilled in the art" reading GUNTOORI et al would obtain from that reference no suggestion to use only the aminoguanidine dimesylate.

Applicants believe that all claims now presented are in condition for allowance and a response to that effect is earnestly solicited.

Applicants enclose a petition to obtain a three month extension of the term for response and enclose Form PTO 2038 to facilitate payment of the fee for the extension through the credit card of the undersigned attorneys.

Respectfully submitted,
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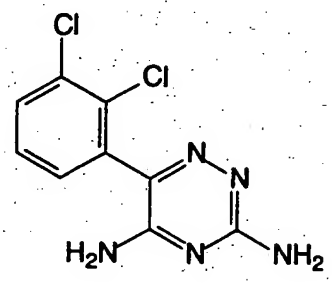
Enclosures: New Abstract of the Disclosure
Substitute Specification
Marked up Version
Petition for Extension
Form PTO 2038

ABSTRACT OF THE DISCLOSURE

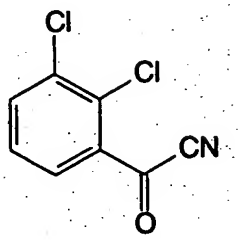
A new process is disclosed for the synthesis of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine of formula (I)



I

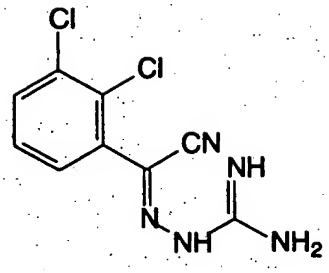
which comprises the steps of:

(a) transforming 2,3-dichlorobenzoyl cyanide of formula (II)



II

with 1-2 mol equivalent of an aminoguanidine salt in 3-6 mol equivalent of methanesulfonic acid to obtain an adduct of the Formula (IV)



IV

and,

(b) then transforming the obtained adduct of formula (IV) without isolation with magnesium oxide, to obtain the compound of the Formula (I).